IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	RICHTER, Mark M. *et al.*
Serial No:	09/074,472
Filed:	May 7, 1998
For:	ASSAYS EMPLOYING ELECTROCHEMILUMINESCENT LABELS AND ELECTROCHEMILUMINESCENCE QUENCHERS
Art Unit:	1634
Examiner:	Arun K. Chakrabarti

RESPONSE UNDER 37 CFR §1.116

Assistant Commissioner for Patents
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Dear Sir:

This reply is in response to the Final Rejection dated November 4, 2002 which has a shortened statutory period for response of three months that expires on February 4, 2003.

REMARKS

In view of the comments which follow, and pursuant to 37 CFR §1.116, reconsideration of the official action dated November 4, 2002 is respectfully requested by Applicants. This response is being submitted within 2 months of the date of the final rejection.

Rejection 1 under 35 USC §103 (a)

Claims 30-31 have been rejected under 35 USC §103 (a) as being unpatentable over U.S. Patent 6,132,955 issued October 17, 2000 to Talley *et al.* (hereinafter "Talley") in view of U.S. Patent 5,798,276 issued August 25, 1998 to Haugland *et al.* (hereinafter "Haugland") and further in view of U.S. Patent 4,743,535 issued May 10, 1988 to Carrico (hereinafter "Carrico").

The Examiner argues that Talley teaches a method for quantitative electrochemiluminescence detection of an oligonucleotide target analyte in a sample, the method comprising the steps of:

1. preparing an assay mixture comprising the sample, one or more assay reagents comprising a labeled complex comprising an ECL label selected from ruthenium bipyridine complexes and osmium bipyridine complexes attached to an oligonucleotide probe complementary to the analyte and capable of hybridizing therewith, the label capable of generating a detectable ECL emission, wherein the labeled complex is immobilized on a magnetic particle, and a coreactant,

2. bringing the assay mixture into contact with a working electrode,

3. applying a potential to the electrode, thereby enabling an ECL reaction to proceed,

4. separating unhybridized labeled complex from hybridized complex,

5. measuring the ECL emission produced by the label hybridized to the analyte via the oligonucleotide probe, and

6. correlating the measured ECL emission with the amount of the analyte in the sample.

The Examiner states that Talley does not teach a method wherein the reagent comprises at least one moiety selected from the group consisting of phenol and benzoquinone.

Haugland, the Examiner argues, teaches a method wherein the reagent comprises at least one moiety selected from the group consisting of phenol and benzoquinone.

It is the Examiner's position that it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to include the group of chemicals containing phenol of Haugland in the method of Talley, since Haugland states "**Dyes** that are able to preferentially bind to a specific biological ingredient in a sample enable the researcher to determine the presence or quantity of that specific ingredient. In addition, specific cellular structures can be monitored with respect to their spatial and temporal distribution in diverse environments. Many applications utilize chemically reactive **fluorescent dyes** by chemically attaching the **dye** to reactive sites on a wide variety of materials such as cells, tissues, proteins, antibodies, enzymes, drugs, hormones, lipids, nucleotides, nucleic acids, or natural or systhetic polymers to make fluorescent conjugates." The Examiner argues that an ordinary practitioner would have been motivated to combine and compare "the **electrochemiluminescence quenching chemicals** containing deferentially substituted phenol ring of Haugland" into the method of Talley in order to achieve the express advantages, as noted by Haugland, of **dyes** that are able to preferentially bind to a specific biological ingredient in a sample, which enables the researcher to determine the presence or quantity of that specific ingredient and

in addition, to monitor specific cellular structures with respect to their spatial and temporal distribution in diverse environments and in addition has many applications that utilize chemically reactive **fluorescent dyes** by chemically attaching the **dye** to reactive sites on a wide variety of materials such as cells, tissues, proteins, antibodies, enzymes, drugs, hormones, lipids, nucleotides, nucleic acids, or natural or synthetic polymers to make fluorescent conjugates.

The Examiner states that Talley in view of Haugland do not teach the combination of **dyes** containing ECL quenching moiety and ECL inducing moiety. (Boldface emphasis added by Applicants.)

The Examiner argues that Carrico teaches the combination of dyes containing ECL quenching moiety and ECL inducing moiety (Column 2, lines 34-54).

It is the Examiner's position that it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the combination of dyes containing ECL quenching moiety and ECL inducing moiety of Carrico in the method of Haugland in view of Talley since Carrico states, "It is proposed to employ a pair of probes which hybridize to contiguous regions on a polynucleotide sequence of interest and to label one probe with a chemiluminescent catalyst such as the enzyme peroxidase and the other with an absorber molecule for the chemiluminescent emission. The catalyst and absorber labels must be situated near the contiguous terminal ends of the respective probes such that upon hybridization there is observed quenching of the chemiluminescent emission by energy transfer to the absorber molecule." The Examiner argues that an ordinary practitioner would have been motivated to combine and substitute the combination of dyes containing ECL quenching moiety and ECL inducing moiety of Carrico in the method of Haugland in view of Talley in order to achieve the express advantages, as noted by Carrico, of a method which provides probes such that upon hybridization there is observed quenching of the chemiluminescent emission by energy transfer to the absorber molecule.

Applicants argue that the Examiner's case for *prima facie* obviousness has not been made. Applicants argue that there must be a basis in the art for combining or modifying references, and that the Examiner has improperly combined the teachings of the references because, once combined, either their intended function is destroyed and/or there is no reasonable expectation of success. Further, Applicants argue that all claim limitations must be considered, especially when missing from the prior art. None of the references cited, either singly or combined, teach or suggest an electrochemiluminescence quenching moiety selected from the group consisting of phenol and benzoquinone, which is required by Applicants' invention.

The Examiner argues (page 4, first paragraph of official action) that "Talley et al do not teach a method wherein the reagent comprises at least one moiety selected from the group consisting of phenol and benzoquinone." Applicants point out that Talley doesn't even teach the concept of an **electrochemiluminescence quenching moiety** as required by Applicants' invention.

The Examiner argues (page 4, second paragraph of official action) that "Haugland et al. teach the method wherein the reagent comprises at least one moiety selected from the group consisting of phenol and benzoquinone (column 2, line 52 to column 3, line 15). Applicants point out, as the Examiner admits, that Haugland teaches **organic reactive dyes**. The ruthenium bipyridine and osmium bipyridine complexes comprising Applicants electrochemiluminescent label are **not dyes**. There is no teaching or suggestion in either Talley or Haugland that dyes and metallic complexes are interchangeable. In fact, one skilled in the art to which the present invention pertains, i.e., the art of electrochemiluminescent immunoassays using a metallic complex label, would not presume that organic dyes are interchangeable with metallic complexes or even operable with metallic complexes, nor would the skilled artisan look to the art of fluorescent, organic dyes to solve problems relating to electrochemiluminescent labels comprising metallic ruthenium or osmium bipyridine complexes.

In his argument, the Examiner states (on page 4, line 18 of the instant office action), "An ordinary practitioner would have been motivated to combine and compare the electrochemiluminescence quenching chemicals containing deferentially substituted phenol ring of Haugland et al. into the method of Talley et al...). Applicants point out that Haugland does not teach "electrochemiluminescence quenching chemicals." Haugland teaches organic, fluorescent dyes. (See Haugland abstract.) Further, Haugland teaches "dyes that are able to preferentially bind to a specific biological ingredient in a sample, which enables the researcher to determine the presence or quantity of that specific ingredient ..." Applicants point out that such compounds are known to the skilled artisan as "**labels**." In Applicants' invention, an **electrochemiluminescent label** is recited; Haugland, on the other hand, teaches **fluorescent labels**.

The Examiner continues to argue, on page 5, first and second paragraphs of the official action, that "Talley et al in view of Haugland et al do not teach the combination of **dyes** containing ECL quenching moiety and ECL inducing moiety. Carrico teaches the combination of **dyes** containing ECL quenching moiety and ECL inducing moiety (column 2, lines 34-54).

Applicants point out, first, that Carrico does not teach "dyes containing ECL quenching moiety and ECL inducing moiety." Carrico teaches (column 2, lines 40-42) a chemiluminescent catalyst, e.g., peroxidase, and an absorber molecule for the chemiluminescent emission. Furthermore, assuming one did attempt to substitute the chemiluminescent catalyst and absorber molecule taught by Carrico into the method of Talley in view of Haugland, the "dye system" of Carrico is incapable of being separated and measured as required by Applicants invention. In column 2, lines 34-37, Carrico teaches that a feature of the hybridization technique being described "dispenses with the need to physically separate hybridized from unhybridized probe."

None of the references cited, Talley, Haugland, and Carrico, teach an electrochemiluminescence quenching moiety selected from the group consisting of

phenol and benzoquinone, which is required by Applicants' invention. There is no suggestion or motivation to even try Haugland's dye conjugates having reactive functional groups including phenols with the method of Talley, nor are Haugland's dye conjugates having reactive functional groups including phenols even expected to be functional if combined with Talley. The addition of Carrico to the combination of references still does not teach or suggest an electrochemiluminescence quenching moiety selected from the group consisting of phenol and benzoquinone, which is required by Applicants' invention.

For reasons set forth herein, therefore, Applicants argue that the Examiner's case for *prima facie* obviousness has not been made. Applicants argue that there must be a basis in the art for combining or modifying references, and that the Examiner has improperly combined the teachings of the references because, once combined, either their intended function is destroyed and/or there is no reasonable expectation of success. Further, Applicants argue that all claim limitations must be considered, especially when missing from the prior art. None of the references cited, either singly or combined, teach or suggest an electrochemiluminescence quenching moiety selected from the group consisting of phenol and benzoquinone, which is required by Applicants' invention.

Applicants respectfully request the Examiner's reconsideration of his rejection of claims 30-31 under 35 USC §103 (a).

Rejection 2 under 35 USC §103 (a)

Claims 30-33 have been rejected under 35 USC §103 (a) as being unpatentable over Talley in view of Haugland further in view of Carrico and further in view of Stratagene Catalog (1988, page 39, hereinafter "Stratagene").

The Examiner argues that Talley in view of Haugland and further in view of Carrico expressly teaches the method claims and assay reagents of claims 30-31, as described in Examiner's argument above. Talley in view of Haugland and further in view

of Carrico does not teach the motivation to combine all the reagents for detecting an analyte in a sample in the form of a kit. Stratagene teaches a motivation to combine reagents into kit format.

It is the Examiner's position that it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a suitable container, ECL label and ECL quenching moiety of Talley in view of Haugland and further in view of Carrico into a kit format as discussed by Stratagene since Stratagene teaches a motivation for combining reagents for use in an assay into a kit.

Applicants argue that the Examiner's case for *prima facie* obviousness has not been made. Applicants repeat their arguments from above that there must be a basis in the art for combining or modifying references, and that the Examiner has improperly combined the teachings of the references because, once combined, either their intended function is destroyed and/or there is no reasonable expectation of success. As with Talley, Haugland, and Carrico, the Stratagene reference also does not teach or suggest an electrochemiluminescence quenching moiety selected from the group consisting of phenol and benzoquinone, which is required by Applicants' invention. Further, Applicants argue that all claim limitations must be considered, especially when missing from the prior art. None of the references cited, either singly or combined, teach or suggest an electrochemiluminescence quenching moiety selected from the group consisting of phenol and benzoquinone, which is required by Applicants' invention.

Applicants respectfully request the Examiner's reconsideration of his rejection of claims 30-33under 35 USC §103 (a).

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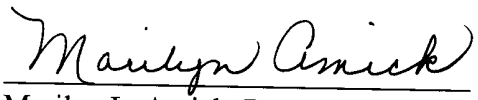
Applicants submit that their application is in condition for allowance, and favorable reconsideration of their application in light of the above remarks is respectfully requested. Allowance of claims 30-33 at an early date is earnestly solicited.

The Examiner is hereby authorized to charge any fees associated with this amendment to Deposit Account No. 02-2958. A duplicate copy of this sheet is enclosed.

Respectfully submitted,

December 16, 2002



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